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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/437,458	11/10/99	GIORDANO A	50093/014001

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EXAMINER	
LEFFERS JR,G	
ART UNIT	**PAPER NUMBER**
1636	5

DATE MAILED: 05/23/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/437,458	Applicant(s) Giordano, et al.
	Examiner Gerald G. Leffers Jr.	Group Art Unit 1636

☐ Responsive to communication(s) filed on _____.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-11* is/are pending in the application.

Of the above, claim(s) *4-11* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-3* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☒ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Specification

1. Claim 1 is objected to because of the following informalities: the identified sequences are not referred to properly. It would be remedial to amend the claim to read "....of the sequences of SEQ ID NOS: 1-20...". Appropriate correction is required.

Election/Restriction

2. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-3, drawn to a nucleic acid sequence which mediates RNA binding protein (RBP) binding activity or mediates the functionality of an mRNA, classified in class 536, subclasses 23.1, 24.1 .

II. Claims 4-8 , drawn to a method of identifying an optimized nucleic acid sequence and an identified, optimized nucleic acid sequence, classified in class 435, subclasses 91.21, 6.

III. Claims 9-10, drawn to methods of identifying a candidate compound affecting an RNA/RNA binding protein pair, classified in class 435, subclass 6.

IV. Claim 11, drawn to a method of identifying an RNA binding protein, classified in class 435, subclass 6; class 436, subclass 501.

The inventions are distinct, each from the other because of the following reasons:

Inventions of Group I and Groups II-IV are related as product and processes of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the nucleic acids of Group I can be used in each of the methods of Groups II-IV.

Inventions of Groups II-IV are biologically and functionally different and distinct from each other and thus one does not render the other obvious. The methods of Groups II-IV comprise steps not required for or present in the methods of the other groups: isolating subfragments from a parent nucleic acid sequence (Group I), contacting an RNA/RNA-binding protein pair with a test compound (Group II) and contacting a known RNA molecule with a test RNA-binding protein (Group III). The end results of the different methods are also different: identification of an optimized subfragment of a parental nucleic acid sequence which retains ~equivalent activity to the parent (Group I), identification of a test compound which appears to affect RNA/RNA-binding protein interaction (Group II) and identification of an RNA-binding protein which interacts with a particular RNA molecule (Group III). Thus, the operation, function and effects of these different methods are different and distinct from each other. Therefore, the inventions of these different, distinct groups are capable of supporting separate patents.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, and because the non-patent literature search required for each of Groups II-IV is not required for or coextensive with the other groups (e.g. isolation of subfragment nucleotide sequences from a parental sequence (Group I), methods of screening test compounds for their effect on RNA-protein interactions (Group II)), restriction for examination purposes as indicated is proper.

This application contains claims directed to the following patentably distinct species of the claimed invention: for each of the Groups please pick one member of SEQ ID NOS: 1-20.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 1-3 are generic for Group I. Claims 4-8 are generic for Group II and claims 9-10 are generic for Group III. Claim 11 is generic for Group IV.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after

the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

During a telephone conversation with Kristine Bieker-Brady on or about 5/12/00 a provisional election was made with traverse to prosecute the invention of Group I, claims 1-3 (SEQ ID NO: 20). Affirmation of this election must be made by applicant in replying to this Office action. Claims 4-11 (and SEQ ID NOS: 1-19) are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claim Rejections - 35 USC § 101

3. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1 and 3 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claims 1 and 3 read on products of nature, such as nucleic acids within an organism which have not been purified or isolated. It would be remedial to amend the claim language to clearly indicate that the specified nucleic acid sequence has been isolated or purified and thus has seen the "hand of man" in its preparation.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-3 are drawn toward a nucleic acid sequence comprising any one of the nucleic acid sequences of SEQ ID NOS: 1-20, or a subfragment derivative thereof, wherein an mRNA

molecule comprising the derived sequence has an RNA binding protein (RBP) binding activity or has an altered or regulated functionality. Claim 3 and specification disclose that the term "regulation of mRNA functionality" comprises an alteration in pre-mRNA processing or in the stabilization, translational efficiency, localization, sequestration, editing, or splicing functions of said mRNA. As written the claims use open claim language that encompasses any nucleic acid which might contain a derivative of one of SEQ ID NOS: 1-20, including genomic DNA sequences, full open reading frames, fusion constructs, etc. Moreover, the claim is also extremely broad in that it encompasses "subfragments" of unspecified length relative to the parental sequence which are "derived" from SEQ ID NOS: 1-20. The claims and specification do not specify how much of the parental sequence is required in order to constitute a "derivative" of one of SEQ ID NOS: 1-20. Claims 1-3 are thus very broad genus claims.

In the specification, SEQ ID NOS: 1-20 are described as being identified as untranslated RNA sequences from the known sequences (obtained from public databases) of biologically important genes and which have specific RBP-binding activity (page 10, line 7). The specification does not disclose which RBPs are in fact bound by any one of the identified sequences. The specification does not disclose for any one of SEQ ID NOS: 1-20 where it is located within the context of the gene with which it is associated. The specification does not disclose whether any one of SEQ ID NOS: 1-20 affects the functional characteristics of the mRNA with which it is associated. The specification does not disclose a common structural feature among the sequences identified in SEQ ID NOS: 1-20, nor does it disclose a common

structural feature for the "derivatives" of any one of SEQ ID NOS: 1-20. There is no guidance in the specification as to what may be the "optimized" sequences for any one of SEQ ID NOS: 1-20 and no relevant examples in which the specified sequences have been "optimized".

Because the claimed genus is extremely broad, because there is no disclosure in the specification as to which portions of SEQ ID NOS: 1-20 bind RBPs and no relevant example of where one of the identified sequences has been used to bind an RBP or alter an mRNAs' functional characteristics and because one cannot predict based on the teachings of the specification or the prior art as to what changes in one of SEQ ID NOS: 1-20 will allow binding of an RBP or allow regulation of an mRNAs' functional characteristics, one of skill in the art would not be able to visualize a representative number of all of the nucleic acids encompassed by claims 1-3. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicants were not in possession of the claimed inventions.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite in that the metes and bounds of the phrase "..or a subfragment nucleic acid sequence derived from any one of the sequences of SEQ ID NOs 1-20..." are unclear. It is unclear as to what exactly constitutes a derivative of one of the identified nucleic acid sequences. For example, would a nucleic acid sequence comprising a nucleotide "derived from" one of the identified sequences constitute a derivative? It would be remedial to amend the claim language to clearly indicate what is intended by the limitation of a "derivative" of one of SEQ ID NOS: 1-20.

Claim 1 is vague and indefinite in that there is no clear and positive prior antecedent basis for the term "said mRNA". The claim recites "..wherein an mRNA molecule...". It would be remedial to amend the claim to provide prior antecedent basis for the term "said mRNA".

Claim 1 is vague and indefinite in that there is no clear and positive prior antecedent basis for the term "said sequence" in claim 1. It is unclear as to whether the term refers to the first nucleic acid sequence or the one derived from one of SEQ ID NOS: 1-20. It would be remedial to amend the claim language to avoid this ambiguity.

Claim 1 is also vague and indefinite in that the metes and bounds of the phrase "..wherein an mRNA molecule comprising said sequence has RNA binding protein (RBP) binding activity or regulates the functionality of said mRNA." are unclear. As written, it is unclear as to whether

the RBP binding activity of the recited nucleic acid sequence must be due to the presence of the nucleic acid sequence (or derivative thereof) of one of SEQ ID NOS: 1-20, or whether the RBP binding activity may be one already associated with the mRNA molecule. Also, it is unclear as the claim is currently written as to whether the presence of the nucleic acid sequence (or a derivative thereof) of one of SEQ ID NOS: 1-20 is necessarily responsible for regulation of the functionality of the mRNA molecule. Upon reading the specification, it appears applicants intend to mean that the presence of one of the nucleic acid sequences (or a derivative thereof) of SEQ ID NOS: 1-20 in an mRNA molecule is directly related to its ability to specifically bind a particular RNA-binding protein or is related to its functional characteristics. It would be remedial to amend the claim language to clearly link the presence of one of the nucleic acid sequences (or derivative thereof) of SEQ ID NOS: 1-20 in an mRNA molecule to its ability to either bind an RNA-binding protein and to directly link the presence of such a sequence to the functional characteristics of the RNA molecule.

Claim 2 is vague and indefinite in that the metes and bounds of the term "optimized" are unclear. The use of the term is unclear in that the characteristics for which the nucleic acid sequence have been optimized are not specified in the claim. Upon reading the specification it appears applicants intend the term to mean that a minimal sequence associated with the identified nucleic acid sequence which is required for RBP-binding activity or for a desired functional characteristic has been identified. It would be remedial to amend the claim language to clearly

indicate what characteristics (e.g. minimal functional length) are encompassed by the term "optimized".

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-3 are rejected under 35 U.S.C. 102(a) as being clearly anticipated by Nagle et al (U) or Gunn et al (V), as evidenced by either Results 1or 2, respectively of the attached Search Report for SEQ ID NO: 20 (W).

The specification discloses that sequences identified in SEQ ID NOS: 1-20 were originally identified from publicly available database sequences as untranslated RNAs (UTRs) and subsequently amplified from cellular DNA by PCR amplification. (page 10, lines 10-page 11, line 5). The specification discloses that the Accession Number used to identify the sequence specified in SEQ ID NO: 20 is #AF116897 which provides the gene sequence for the mouse mahogany gene.

Nagle et al teach the identification of the mouse mahogany (mg) gene. Nagle et al teach that the cDNA sequence for mahogany was deposited at Genbank by their group under Accession Number AF116897 (Abstract; page 152, last line of the paper).

Gunn et al also teach the identification of the mouse mahogany locus, which they name as Mgca (Abstract). Gunn et al teach that the genomic sequence for Mgca was deposited by their group at GenBank under Accession Numbers AF120317 and AF120318 (page 156, last line of the paper).

Extrinsic evidence that the nucleic acid sequences deposited by Nagle et al and Gunn et al are (or comprise) sequences which, when present in an mRNA molecule, will provide either RNA binding protein (RBP) binding activity to said mRNA or alter a functional characteristic of said mRNA molecule is provided by the Search Report for SEQ ID NO: 20. Result 1 shows 100% identity across the length of SEQ ID NO: 20 to the sequence provided by Nagle et al, which is as expected since the sequence submitted by Nagle et al (Accession Number AF116897) is the one disclosed in the specification as the source of the sequence recited in SEQ ID NO: 20. The search report teaches that the sequence given in Accession Number AF116897 was publicly available on 20 March 1999. Similarly, Result 2 of the Search Report for SEQ ID NO: 20 discloses that there is a 98.1% identity match for SEQ ID NO: 20 to the sequence disclosed by Gunn et al in Accession Number AF120318. The search report teaches that the sequence provided to GenBank by Gunn et al was publicly available on 31 March 1999.

Conclusion

No claims are allowed.

Certain papers related to this application may be submitted to Art Unit 1636 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone numbers for the Group are (703) 308-4242 and (703) 305-3014. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gerald Leffers, Jr. whose telephone number is (703) 308-6232. The examiner can normally be reached on Monday through Friday, from about 9:00 AM to about 5:30 PM. A phone message left at this number will be responded to as soon as possible (usually no later than 24 hours after receipt by the examiner).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. George Elliott, can be reached on (703) 308-4003.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

GLJ

G. Leffers, Jr.

Patent Examiner

Art Unit 1636

May 22, 2000

TERRY MCKELVEY
PRIMARY EXAMINER

09/437,458 Attach Paper #5

0	xavier-asish$.in.
0	xavier-ashish$.in.
10	giordano-anthony$.in.
18	xavier-a$.in.
54	giordano-a$.in.
0	mahogany.in.
2547	transcription$ with regulation
67	7 with cis
43	7 with cis with sequence
111	7 with method
4	10 with cis
0	10 with (untranslated)
2762	rna with (stability or processing)
137	13 with method
9	14 with expression

09/437,458
Attach Paper #5

(FILE 'HOME' ENTERED AT 14:38:38 ON 17 MAY 2000)

FILE 'MEDLINE, EMBASE, BIOSIS, CAPLUS' ENTERED AT 14:39:22 ON 17 MAY 2000

L1	1613	S (GIORDANO, A?)/IN,AU
L2	2	S (GIORDANO, ANTHONY)/IN,AU
L3	697	S (XAVIER, A?)/IN,AU
L4	0	S (XAVIER, ASISH?)/IN,AU
L5	0	S (XAVIER, AS?)/IN,AU
L6	2310	S L1 OR L2 OR L3
L7	62	S L6 AND RNA
L8	9	S L6 AND (RNA (S) BINDING)
L9	6	DUPLICATE REMOVE L8 (3 DUPLICATES REMOVED)
L10	0	S L6 AND RBP
L11	64	S L6 AND (TRANSCRIPTION? (2W) REGULATION)
L12	32	DUPLICATE REMOVE L11 (32 DUPLICATES REMOVED)
L13	0	S L3 AND (RNA (S) BINDING)
L14	0	S L3 AND L1
L15	0	S L3 AND ASHISH
L16	5	S L3 AND RNA
L17	4	DUPLICATE REMOVE L16 (1 DUPLICATE REMOVED)
L18	127890	S TRANSCRIPTION? (S) REGULATION
L19	5360	S L18 (S) CIS
L20	5	S L18 AND MAHOGANY
L21	3	DUPLICATE REMOVE L20 (2 DUPLICATES REMOVED)